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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/597,946	09/01/2006	Roger Michael Lane	33659-US-PCT	8266

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NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
POLANSKY, GREGG	

ART UNIT	PAPER NUMBER
1611	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/597,946	LANE, ROGER MICHAEL	
	Examiner	Art Unit	
	Gregg Polansky	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/14/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Applicant's Information Disclosure Statement, filed 8/14/2006, is acknowledged and has been reviewed to the extent each is a proper citation on a U.S. Patent. Documents not considered were those which were not provided by Applicant and were unavailable to the Examiner.

2. Claims 1-32 are pending and presently under consideration.

Specification

3. The use of numerous trademarks has been noted in the Specification. For example, see page 4, 2nd paragraph from the bottom. They should be written in all capital letters wherever it appears; or alternatively, it should be denoted with the registered trademark symbol, ®, and be accompanied by the generic terminology.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 2, 16-18, 21 and 28-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2 and 21 are drawn to a method of treating "late-onset" vascular depression, which renders the claim indefinite. It is unclear what constitutes "late-onset"

vascular depression. There is no teaching in the Specification as to what constitutes "late-onset" with regard to vascular depression, making it impossible to ascertain with reasonable precision when the claim is infringed and when it is not.

Claim 16 recites the abbreviations "SSRI" and "MAO". The first use of an abbreviation in the claims should be preceded by a full recitation of the abbreviated term so it is clear exactly what the abbreviation means.

Claims 17 and 18 contain the trademark names of anti-depressants without their corresponding generic names. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See Ex parte Simpson, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present claims, the trademarks do not adequately identify each anti-depressant.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the

applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 9 and 32 are rejected under 35 U.S.C. 102(e) as being anticipated by Seed, J. (U.S. Patent Application Pub. No. 2005/0143350 A1).

Seed teaches *inter alia* pharmaceutical compositions comprising at least one cholinesterase inhibitor, at least one antidepressant and a pharmaceutically acceptable carrier. See Abstract; page 5, paragraph 50; and page 22, claim 40. Seed discloses the pharmaceutical compositions taught in the reference can be provided in a kit (e.g., commercial package). The cholinesterase inhibitors and antidepressants are provided in the kit as separate or combined formulations. See Abstract and pages 7-8, paragraphs 66-69. No patentable weight is given to printed matter absent a new and unobvious functional relationship between the printed matter and the substrate. See *In re Ngai*, 367 F.3d 1336, 1339, 70 USPQ2d 1862, 1864 (Fed. Cir. 2004).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 9-19 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seed, J. (U.S. Patent Application Pub. No. 2005/0143350 A1), in view of Hsu et al. (U.S. Patent Application Pub. No. 2002/0192243 A1).

Seed teaches pharmaceutical compositions comprising at least one cholinesterase inhibitor, at least one antidepressant and a pharmaceutically acceptable carrier (*supra)*. Seed teaches the instantly claimed cholinesterase inhibitors (i.e., donepezil, rivastigmine, galanthamine) and typical doses. See pages 2-3, paragraph 24 and page 3, paragraph 29. The reference teaches the dosages of the active agents are "in accordance with dosages and scheduling regimens practiced by those of skill in the art". Seed teaches, for example rivastigmine can be administered in a dose range of 0.4 mg to about 6.0 mg/dose and up to 12.0 mg/day. Seed teaches suitable antidepressant classes include *inter alia* tricyclics, SSRIs, SNRIs, and MAO inhibitors.

Seed also teaches the instantly claimed individual antidepressants, such as sertraline, fluoxetine, venlafaxine, and citalopram. See for example, page 4, paragraphs 32 and 34. The reference teaches the composition may be administered by transdermal patch. See page 1, paragraph 12, and page 5, paragraph 51.

Seed discloses the pharmaceutical compositions taught in the reference can be provided in a kit (e.g., commercial package). The cholinesterase inhibitors and antidepressants are provided in the kit as separate or combined formulations (*supra*).

The reference by Hsu et al. is provided to demonstrate administration of cholinesterase inhibitors by transdermal patch was known at the time of the instant invention. The reference also teaches methods for enhancing the permeability of skin to transdermal application of cholinesterase inhibitors, while minimizing local skin irritation. See Abstract and page 6, paragraph 67. Hsu et al. teach transdermal patch surface area in the range of about 5-200 cm^2, which encompasses the range recited by

instant Claims 14 and 15. See page 10, paragraph 101. The concentration of the drug (e.g., rivastigmine) is dependent on the desired daily dose to be administered, the size of the patch and the flux rate of the drug.

Hsu et al. also disclose that for transdermal administration, the cholinesterase inhibitor compounds should be "(1) an uncharged molecule, e.g., wherein a basic drug is in nonionized, free-base form, (2) a basic salt of an acidic drug, or (3) there are no additional species in the formulation or patch that could react with or be neutralized by the inorganic hydroxide, to any significant degree a free base form of the cholinesterase inhibitor and to improve the flux of the drug". See Abstract and page 5, paragraphs 43 and 44.

Further, Hsu et al. disclose the instantly claimed cholinesterase inhibitor salts (i.e., donepezil HCl, galanthamine HBr, and rivastigmine tartrate). See page 6, paragraph 67.

One would have been motivated to combine the teachings of Seed with those of Hsu et al. at the time of the invention because Hsu et al. teach methods for enhancing the flux of the cholinesterase inhibitors and for minimizing skin irritation from the transdermal application. Also, whereas Seed teaches unspecified salts of cholinesterase inhibitors (page 5, paragraph 50), Hsu et al. teach specific exemplary salts (*supra*).

Seed or Hsu et al. do not teach a specific amount of rivastigmine in a transdermal patch of the sizes recited by instant Claims 14 and 15. However, Seed does teach the administration of rivastigmine in the same dose range as disclosed for

the instant invention and Hsu et al. does teach a patch size range that encompasses the sizes recited for the instant invention.

The determination of both optimal dosage ranges and optimal modes of administration are parameters easily determined by those skilled in the art through no more than routine experimentation. Since the instant claims are drawn to compositions, one of ordinary skill would have modified the dose as required by the condition being treated. It is not inventive to discover the optimum or workable ranges by routine experimentation when general conditions of a claim are disclosed in the prior art. See *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233,235 (CCPA 1955) and MPEP 2144.05(11). The determination of the optimum dosage regimen (i.e., patch composition amount and patch dimensions) to employ with the presently claimed active agents would have been a matter well within the purview of one of ordinary skill in the art.

10. Claims 1-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roman et al. (The Lancet Neurology, 2002, Vol. 1, pages 426-436 [cited on IDS but publication not provided by Applicant]), in view of Seed, J. (U.S. Patent Application Pub. No. 2005/0143350 A1), and Hsu et al. (U.S. Patent Application Pub. No. 2002/0192243 A1).

Claims 1-8 and 20-31 are drawn to methods of treating vascular depression, Claims 9-19 are drawn to pharmaceutical compositions comprising a cholinesterase inhibitor, and an antidepressant, and Claim 32 is drawn to a commercial package (kit). Claims 2 and 21 recite the limitation of "late onset" vascular depression. However,

since there is no disclosure as to what "late onset" encompasses, it is not possible to evaluate this limitation or to determine if any art reads on it.

Roman et al. teach clinical manifestations of vascular dementia include vascular depression. See page 431, 1st column, 2nd to last paragraph, and page 432, "Panel 3. Criteria for SIVD". Roman et al. disclose the use of cholinesterase inhibitors, including donepezil hydrochloride, rivastigmine tartrate, and galantamine hydrobromide, for the treatment of vascular dementia and the concomitant use of antidepressants, in particular serotonin-specific reuptake inhibitors (SSRIs) (e.g., sertraline and citalopram), for the treatment of depression which accompanies vascular dementia. See page 434, "Cholinesterase inhibitors" and "Other agents".

Although Roman et al. teach the combined use of a cholinesterase inhibitor (e.g., rivastigmine) and an antidepressant (e.g., setraline) for treating vascular depression, they do not teach a cholinesterase inhibitor and an antidepressant formulated together or the administration of rivastigmine by transdermal patch. The reference is also silent on a commercial package as required by instant Claim 32.

Seed teach combined preparations of cholinesterase inhibitors and antidepressants, the use of a transdermal patch as a method for administration of the preparations and the use of a kit (package) for distributing the compositions (*supra*).

The teachings of Hsu et al. are provided *supra*.

As discussed *supra*, Seed or Hsu et al. do not teach a specific amount of rivastigmine in a transdermal patch of the sizes recited by instant Claims 7, 8, 14 and 15. However, Seed does teach the administration of rivastigmine in the same dose

range as disclosed for the instant invention and Hsu et al. does teach a patch size range that encompasses the sizes recited for the instant invention.

It would have been well within the purview of one of ordinary skill in the art to formulate a transdermal patch to administer therapeutic doses of rivastigmine. One would have been so motivated to provide a more convenient method of administration, as well as a means of providing extended release of the medicament and improving patient compliance.

It would have been obvious to the skilled artisan to initiate administration of the active agents at a low dose and gradually increase the dose to a level that is determined by patient response and route of administration. One would have been motivated to do so to effectively treat the patient while minimizing potential drug side effects.

As presented above, the determination of both optimal dosage ranges and optimal modes of administration are parameters well within the purview of those skilled in the art through no more than routine experimentation. The determination of the optimum dosage regimen (i.e., patch composition amount and patch dimensions) to employ with the presently claimed active agents would have been a matter well within the purview of one of ordinary skill in the art.

It would have been obvious to of one skilled in the art to package pharmaceutical compositions in a kit. One would have been motivated to do so effectively and efficiently distribute the pharmaceutical compositions.

Conclusion

11. Claims 1-32 are rejected.

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregg Polansky whose telephone number is (571)272-9070. The examiner can normally be reached on Mon-Thur 9:30 A.M. - 7:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gregg Polansky/
Examiner, Art Unit 1611

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1614